Disease Name — Homocystinuria

Alternate name(s)	Cystathionine beta-synthase deficiency
Acronym	CBS deficiency
Disease Classification	Amino Acid Disorder
Variants	Yes
Variant name	Pyridoxine-responsive type (the majority of cases are unresponsive to pyridoxine)
Symptom onset	Childhood
Symptoms	Ectopia lentis, vascular occlusive disease, seizures, malar flush, osteoporosis, possible decreased pigmentation of hair, skin and iris, skeletal abnormalities including genu valgum, pectus excavatum, pes cavus and marfanoid habitus. Some patients have failure to thrive and short stature. Mental retardation is possible.
Natural history without treatment	Mental retardation is common but not invariable. Vascular disease, stroke and psychiatric abnormalities.
Natural history with treatment	Decrease of thromboembolic accidents which may decrease incidence of sequelae including mental retardation, ectopia lentis, seizures and psychiatric abnormalities. Normal IQ is possible and typical of the pyridoxine-responsive variant.
Treatment	Pyridoxine supplementation, dietary restriction of methionine with supplementation of L-cysteine, betaine supplementation. Consider folate and vitamin B12 supplementation.
Other	N/A
Physical phenotype	Ectopia lentis, decreased pigmentation, malar flush, osteoporosis, skeletal abnormalities and marfanoid habitus
Inheritance	Autosomal recessive
General population incidence	1:200,000 – 300,000
Ethnic differences	Yes
Population	Irish, U.S New England
Ethnic incidence	1:50,000
Enzyme location	Lymphocytes, fibroblasts and liver
Enzyme Function	Degradation of homocysteine
Missing Enzyme	Cystathionine beta-synthase
Metabolite changes	Increased methionine in blood, increased homocystine in urine, increased total homocysteine in blood.
Gene	CBS gene
Gene location	21q22.3
DNA testing available	Yes
DNA testing detail	Numerous mutations have been detected. Most prevalent mutations are G307S and I278T. Most patients are compound heterozygotes.
Prenatal testing	Enzyme assay in cultured amniocytes (CVS not possible)
MS/MS Profile	N/A
OMIM Link	http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=236200
Genetests Link	www.genetests.org
Support Group	National Coalition for PKU and Allied Disorders http://www.pku-allieddisorders.org/ Children Living with Inherited Metabolic Diseases http://www.climb.org.uk/